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Autonomic function tests in young female obese individuals

KANNAN RAMAIAH¹, M.SIVARAJ², S.PALANI³

¹Associate Professor, Department of Physiology, Madras Medical College, Chennai

² Deputy Director of Medical Education, Directorate of Medical Education, Tamilnādu, Chennai.

³ Assistant Professor, Department of Physiology, Govt. Kilpauk Medical College, Chennai

Corresponding author: Dr. M. Sivaraj, Deputy Director of Medical Education, Directorate of Medical Education Tamilnadu Chennai.



ABSTRACT

Obesity is a leading preventable cause of death worldwide, with increasing prevalence in adults and children. Obesity is a complex disorder characterized by autonomic dysfunction in addition to alteration in sympathetic and parasympathetic activity of the heart. It is being recognized that the autonomic nervous system derangement takes place in obese persons. With this background we studied cardiac autonomic function in young obese female individuals. The study and control group were subjected to battery of autonomic function tests using standard techniques. The cardio vascular autonomic reflexes tests (Orthostatic standing test, Deep Breathing, Valsalva Manoeuvre, Isometric Hand Grip Test and Cold Pressor Test) are considered to predict the autonomic dysfunction if three out of five tests are abnormal. Based on these criteria, our study was able to quantify the autonomic dysfunction in young obese female individuals.

Key words: Obesity, Valsalva Manoeuvre, Isometric Hand Grip, Cold Pressor Test.

INTRODUCTION

Obesity is leading preventable cause of death worldwide, with increasing prevalence in adults and children. Authorities view it as one of the most serious public health problems of 21st century. The increased prevalence of obesity parallels the increase in sedentary life style. The increased consumption of so called junk foods which include pizza, can drinks and other fast foods contribute to obesity in adults and children. Obesity is a complex disorder characterized by autonomic dysfunction in addition to alteration in sympathetic and parasympathetic activity of the heart. It is being recognized that the autonomic nervous system derangement takes place in obese persons. Autonomic Nervous System has been focus of much research activity in recent years in the quest to improve and understand the early pathophysiological process underlying the cardiovascular changes associated with obesity. With this background we studied cardiac autonomic function in young obese female individuals.

AIM OF THE STUDY

To evaluate Cardiovascular Autonomic Dysfunction in obese female subjects by adopting the standard Autonomic Nervous Function Tests.

MATERIALS AND METHODS:

CASES: 30 obese female individuals in the age group of 18 to 25 years, without co-morbid conditions like Diabetes, Hypertension, Smoking, Alcoholism, Thyroid disorders

WHO criteria was applied to categorize the subjects; Controls – subjects with BMI 18.5 – 24.9 and Obese when their BMI is more than 25

CONTROLS

30 age and gender matched healthy, non-obese female subjects attending the Master health check up programme, Madras Medical College & Government General hospital, Chennai.

The study protocol was approved by the Ethical committee of Madras Medical College. Informed and written consent was obtained from the subjects.

The study and control group were subjected to battery of autonomic function tests using standard techniques described by Ewing et-al.^(1,2) It was ensured that the tests were carried out at optimal temperature. Patients were instructed to empty their bladder before testing.

ORTHOSTATIC STANDING TEST:

The subject was asked to stand up in 3 seconds and was allowed to stand for 5 minutes, without any support by putting equal weight on both the legs. Blood pressure and pulse rate was recorded after 1 minute, 2 minutes and 5 minutes. Continuous ECG monitoring was also done. The R-R interval is obtained from 15th beat and 30th beat. The maximum R-R interval at the 30th beat and the minimum R-R interval during 15th beat give the 30/15 ratio..

DEEP BREATHING:

After 15 minutes of rest in sitting position, the subject was asked to take deep breaths at a rate of 6 breaths / min. Inspiratory and expiratory periods were identified with the help of stethographic respiratory tracings recorded in the physiograph connected to polygraph compatible ECG recorder and ECG was also recorded continuously by connecting the ECG leads to the ECG recorder which in turn was connected by the signal processing unit to the computer. The average of longest R-R interval during expiration and shortest R-R interval during Inspiration for the 6 cycles is obtained and from this we calculate the E/I ratio.

$$E/I \text{ ratio} = \frac{\text{Longest R-R interval in Expiration}}{\text{Shortest R-R interval in Inspiration}}$$

VALSALVA MANOEUVRE,

After 15 minutes of rest ,the subject was asked to increase the intrathoracic pressure after normal inspiration, by expiring forcefully into the mouthpiece connected to a mercury manometer, so as to raise the mercury level to 40mmHg and was instructed to maintain this for 15 seconds. After holding for 15 seconds, the pressure was released. During the whole procedure, the ECG and stethographic respiratory tracings were recorded continuously. The 4 phases of the test was identified by using respiratory tracings. The increase in Heart rate during Phase II and decrease in heart rate during Phase IV is noted.⁽³⁾

$$\text{Valsalva ratio} = \frac{\text{Max R-R interval during Phase IV}}{\text{Min R-R interval during Phase II}}$$

ISOMETRIC HAND GRIP TEST:

The baseline blood pressure and heart rate of the subject was recorded. The maximum voluntary contraction of each subject was determined by asking them to press the hand grip dynamometer with maximum force for few seconds and the process was repeated thrice. The maximum of the readings was taken as maximum voluntary contraction (MVC). The subject was asked to maintain 30% of his / her MVC for 3 to 5 minutes. Blood pressures and Heart rate was measured from the opposite limb during the procedure and after 5 min of cessation of the procedure.

COLD PRESSOR TEST:

After 15 minutes of rest the base line blood pressure and heart rate was measured and the subject was asked to immerse his/her hand into water at 4 degrees Centigrade for one minute . The Blood pressure and Heart rate were measured from the opposite limb during the procedure.⁽⁴⁾

All the results obtained from the tests were analyzed statistically using unpaired t test (SPSS version 11 software)

RESULTS:

The data for the different variables were analyzed and the values were expressed as Mean ± SD.

- 'p', value < 0.05 was considered significant.
- 'p', value < 0.01 was considered highly significant,
- 'p' value < 0.001 was considered very highly significant.

The results and their significance are given in the following tables and charts.

TABLE 1

VARIABLES	CONTROLS	OBESE	p value
AGE in years	21.76 ± 4.25	19.37±3.99	0.13
BMI Kg/m2	22. 25 ± 1.09	35.23±5.36	< 0.001

TABLE 2: AUTONOMIC FUNCTION TESTS

	CONTROLS	OBESE	'p' value
Orthostatic standing test [30:15]	1.17 ± 0.08	1.03 ± 0.109	<0.001 Very highly significant
Deep breathing [E:I]	1.20 ± 0.06	1.07 ± 0.067	<0.001 Very highly significant
Valsalva ratio	1.27 ± 0.05	1.19 ± 0.04	<0.001 Very highly significant
Isometric hand grip [DPd- 1min]	7.37 ± 1.97	10.20 ± 1.65	<0.001 Very highly significant
Isometric hand grip [DPd- 5min]	0.50 ± 1.83	1.00 ± 4.39	>0.05 Not significant

Cold pressor test [DPd – 1 min]	6.20 ± 1.35	9.17 ± 2.60	<0.001 Very highly significant
Cold pressor test [DPd – 5 min]	0.5 ± 1.74	0.53 ± 1.655	>0.05 Not significant

DISCUSSION

The cardio vascular system response to different stimuli is assessed by using cardio vascular reflex tests to identify whether parasympathetic component attenuation underlies the sympathetic over activity.

Ortho Static Tests (OST)

Measuring the reflex autonomic responses on assuming of upright posture provides information on the integrity of afferent, central and efferent baroreflex pathways. The ANS responses to active standing and passive tilting are different. Standing produces immediate fall in cardiac output due to gravitational blood pooling.

This is accompanied by an increase in heart rate which is maximum at about 15th beat. Upon active standing, contraction of limbs and abdominal muscles produces a transient increase in venous return and a blood pressure overshoot which peaks at about the 30th heart beat and results in slowing of the heart rate. The ratio of maximum R-R interval to minimum R-R interval (30/15 ratio) is used as a measure of vagal function.

R-R interval between 30th - 31st beat

30/15 th beat ratio = -----

R-R interval between 15th - 16th beat

If the 30:15 ratio (also called postural tachycardia index) was

- 1.04 and above - it was considered normal,
- 1.01 and 1.03 - as borderline and
- 1 or less - as an abnormal response.

In our study the orthostatic standing test showed a significant decrease ($p < 0.001$) in obese subjects (1.03 ± 0.05) compared to the controls (1.17 ± 0.08) indicating a poor parasympathetic response.

Deep Breathing (DB)

The presence of respiratory sinus arrhythmia depends on the integrity of efferent vagal neurons. Inspiration results in increased heart rate and expiration results in decreased heart rate. The E/I ratio is calculated as the ratio of longest R-R interval during expiration to the shortest R-R interval during inspiration when breathing at the rate of 6 breaths per minute. It has been widely accepted as a method to test efferent cardiac vagal function.

$$\text{E:I ratio} = \frac{\text{longest RR interval in expiration}}{\text{shortest RR interval in inspiration}}$$

An E:I ratio of > 1.10 was considered normal
 < 1.10 - as an abnormal response.

E/I ratio showed a significant decrease in obesity subjects (1.07 ± 0.067) compared to the controls (1.20 ± 0.06) there by confirming a decreased parasympathetic activity.

Valsalva Ratio (VR)

The Valsalva Ratio is calculated as the ratio of longest R-R interval during phase IV (bradycardia due to vagal withdrawal) to the shortest R-R Interval during phase II (tachycardia due to sympathetic activation and vagal withdrawal). It measures both the afferent and the efferent vagal reflex arc.

$$\text{Valsalva Ratio} = \frac{\text{longest RR Interval during Phase IV}}{\text{shortest RR Interval during Phase II}}$$

- A Valsalva Ratio Of
- > 1.21 and above - was considered normal
 - > 1.11 and 1.20 - as borderline
 - > 1.10 or less - as an abnormal response

Our study shows that the mean VR of obese subjects were of borderline significance (mean VR= 1.19 ± 0.04). It showed a significant decrease when compared to controls (1.27 ± 0.05) which also proves a decreased parasympathetic response. Though VR is a predictor of both sympathetic and para sympathetic dysfunction, we were not able to predict the sympathetic component as we did not have a beat to beat BP monitoring.

Isometric Hand Grip Test (IHGT)

The response to IHGT is reflex in nature. It is thought to be initiated by the stimulus from the exercising muscle. The strength of the muscle sympathetic activity depends on the baroreflex sensitivity. Hence increased sympathetic activity is needed to sensitize the baroreceptor to bring about the response.

The diastolic pressure difference at the end of one minute increased in the obese subjects (10.20 ± 1.65) compared to the controls (7.37 ± 1.97). This significant increase ($p < 0.001$) suggests an increase in sympathetic activity in obesity subjects in our study, although there was no significant change for the same at the end of five minutes.

Cold Pressor Test (CPT)

This is one of the battery of tests which relates to sympathetic activity. In our study the diastolic pressure difference was significantly higher in the obesity subjects (9.17 ± 2.60) compared to the controls (6.20 ± 1.35). This increase in diastolic blood pressure response in obese patients has been stated to be because of increased vasomotor response. This is due to increased sympathetic outflow by activation of thermal and nociceptor afferents from the immersed hand.

To quantify the autonomic dysfunction, the cardio vascular autonomic reflex tests (DB, VM, OST, IHGT and CPT) are considered to predict the autonomic dysfunction if three out of five tests are abnormal. Based on these criteria, our study was able to quantify the autonomic dysfunction in young obese female individuals. Most of the studies are done using a maximum of only three tests to predict the autonomic dysfunction. Therefore a battery of six tests mentioned in this study will definitely identify the autonomic dysfunction independent of severity of the disease. By evaluating the subjects with a battery of other ANF tests we could identify an increased sympathetic activity by a significant rise in the values of isometric hand grip test and cold pressor test and a parasympathetic blunting as seen in the other tests namely orthostatic standing (30/15 ratio), deep breathing (E : I) and valsalva ratio.

CONCLUSION:

Obesity provokes profound changes in the autonomic nervous system. The mechanism by which these changes occur is complex and is affected by number of different stimuli the most important of which appear to be the recurrent episodes of hypoxaemia, ventilator stress and cortical arousal, the key features of the Obesity syndrome^(5,6). These ANS changes are instrumental in mediating the characteristic acute haemodynamic changes of obesity and it is possible that this contributes to the high cardiovascular risk that sufferers carry. There is mounting evidence that individuals with obesity undergo complex readjustment of autonomic homeostatic mechanisms. They have impaired responses to autonomic stress tests and have high levels of baseline sympathetic activity⁽⁷⁾, even at rest the obese people having increased heart rate when compared to normal individuals. Obesity of its own is associated with labile haemodynamic and autonomic activity. There is therefore strong circumstantial evidence of a causal relationship between obesity and cardiovascular diseases.

Recent advances in understanding the ANS function and its relationship to the pathophysiological events has lead to early recognition of obesity associated cardiovascular morbidity,. With the help of this specific battery of autonomic function tests, we can detect individuals who are prone to develop cardiovascular complications. For diagnostic purposes, it is preferable to perform a battery of tests rather than to rely on a single test to determine if autonomic reflex function is intact. These tests are specific, sensitive safe and widely used for diagnosis and monitoring of autonomic neuropathies.

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